

**REMARKS**

In view of the following remarks, the Examiner is requested to reconsider and allow Claims 1-40, the only claims pending and under examination in this application.

**CLAIM REJECTIONS – 35 U.S.C. §103**

***Claim Rejection over Bockow in view of Edwards***

Claims 1-3, 5-8, 10-12, 14-18, 29, 34-36, 38 and 39 are rejected under 35 U.S.C. §103(a) as allegedly being obvious over Bockow (USPN 5,709,855) in view of Edwards (USPN 5,989,559).

In making the rejection, the Examiner asserts that Bockow's use of a topical composition containing a cyclooxygenase inhibitor for treating pain, in combination with Edwards' treatment of Carpal Tunnel Syndrome (CTS) by applying a topical formulation to the wrist, renders the claims obvious.

As developed below, the claims are patentable over the cited combination of references for at least the following reasons:

- A) One of ordinary skill in the art would not have combined the teachings of the cited references as asserted by the office; and
- B) One of ordinary skill in the art could not have predicted success in the claimed invention prior to the Applicant's work reported in the present application.

Each of these reasons for finding the asserted prima facie case of obviousness to be insufficient is further developed separately below.

**I. No Apparent Reason to Combine References in Manner Suggested by the Office**

As taught in *KSR*, "Courts determining whether claimed combination of elements known in prior art would have been obvious will often be required to look to interrelated teachings of multiple patents, effects of demands known to design community or

present in marketplace, and background knowledge of person of ordinary skill in art in order to determine whether there was apparent reason to combine known elements in manner claimed in patent in suit, and in order to facilitate review, this analysis should be made explicit.....”<sup>1</sup> As such, for a combination of elements to be obvious, there must be some apparent reason to combine the elements of the art in the manner stated in the claims at issue, based on factors including background knowledge of a person of ordinary skill.

Applicants submit that, upon correct determination of the content of the prior art at the time of the invention, there is no apparent and valid reason to combine the teachings of Bockow and Edwards as asserted by the Examiner. As established below, Bockow incorrectly lists CTS as a musculoskeletal disorder. Based on the knowledge of those of skill in the art at the time of the invention, one of ordinary skill in the art would read this mention of CTS by Bockow as an incorrect characterization of CTS and therefore not read Bockow in the manner asserted by the Examiner. Indeed, one of skill in the art would read Bockow as teaching nothing about CTS. Accordingly, the Examiner's asserted motivation to combine Bockow with Edwards is based on Bockow's incorrect characterization of CTS and an incorrect assumption of how one of ordinary skill in the art would read Bockow.

In maintaining his rejection, the Examiner reasons that the prior art methods are still relevant to consider because re-characterization of CTS from a musculoskeletal disorder to a neuropathy has not been shown to lead to a complete abandonment of prior art methods. See Office Action, ¶ bridging pgs 7 and 8.

However, the content of Bockow should be determined at the time of the claimed invention, not at the time Bockow was filed (i.e., September 22, 1995) nor at the present time after learning the claimed invention. At the time the claimed invention was made, it

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<sup>1</sup> *KSR International v. Teleflex Inc.*, 127 S. Ct. 1727, 1739 (2007).

was within the knowledge of one of skill in the art that CTS is a neuropathy<sup>2</sup>, which has an entirely distinct pathology from that of musculoskeletal diseases. As such, one of skill in the art would have noted that Bockow incorrectly list CTS as a musculoskeletal disorder. For this reason, despite that Bockow characterizes CTS as a musculoskeletal disorder, one of skill in the art at the time of the claimed invention, knowing that CTS is not a musculoskeletal disorder, would not have viewed Bockow as teaching a method to treat CTS. Rather, one of skill in the art would have viewed Bockow as teaching treatment of musculoskeletal disorders in general. For that reason, one of skill in the art would not have relied upon Bockow's compositions to treat a neuropathy.

Upon reading Bockow and Edwards, one of ordinary skill in the art cannot reasonably link Bockow's compositions to treat musculoskeletal disorders with Edwards' method for treating CTS, which is known as a neuropathy in the art, with banana peel extracts. Based on the background knowledge at the time of the claimed invention, Bockow provides no apparent reason to use its compositions to treat CTS, because CTS is clearly listed incorrectly as a musculoskeletal disorder.

Accordingly, there is no apparent reason to combine Bockow with Edwards as has been done by the Examiner in making this rejection and this rejection may be withdrawn for this reason alone.

## II. Predicted Success

Applicants submit that the claims are patentable over the cited combination of references because the prior art at the time of filing fails to provide any reasonable expectation of success in the claimed methods.

Case law is replete with examples requiring that there must be predicted success in combining prior art references. The "predicted success" of a combination of elements

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<sup>2</sup> "Carpal tunnel syndrome is the most common neuropathy of the peripheral nerves." See abstract, Bozek M, et al., *Ortop Traumatol Rehabil.* 2001 Sep 30;3(3):357-60.

is an important factor in determining obviousness. This principle is illustrated in *three* Supreme Court cases<sup>3</sup> decided prior to *KSR*, and is a recurring theme of *KSR*. For example, in *KSR*, the Supreme Court stated that in order for a combination of elements to be patentable “the combination must do more than yield a predictable result”.<sup>4</sup> Likewise, the corollary principle, namely that “[t]he combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results”<sup>5</sup> is also discussed. The Supreme Court in *KSR* also stated that that “a court *must* ask whether the improvement is more than the predictable use of prior art elements according to their established functions”.<sup>6</sup>

Consistent with the application of the above four Supreme Court cases, including *KSR*, an invention would be nonobvious unless there was predicted success.

In the previous response dated November 14, 2007, Applicants established that one could not have predicted success based on the combined teachings of these references because:

- Bockow is directed primarily to treating musculoskeletal disorders with an omega fatty acid spirulina formulation;
- Bockow only provides actual exemplification in the treatment of musculoskeletal disorders; and
- Edwards only provides exemplification with banana peel extract compositions.

This assertion by Applicants is based on the background knowledge in the art as evidenced by declarations of record in the present application. The declarations of record establish the following facts:

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<sup>3</sup> *United States v. Adams*, 383 U.S. 39, 40 (1966); *Anderson's-Black Rock, Inc. v. Pavement Salvage Co.*, 396 U.C. 57, 60-62 (1969) and *Sakraida v. AG Pro, Inc.*, 425 U.C. 273, 282 (1976).

<sup>4</sup> *KSR International v. Teleflex Inc.*, 127 S. Ct. 1727, 1740 (2007).

<sup>5</sup> *KSR* at 1739.

<sup>6</sup> *KSR* at 1740; emphasis added.

- CTS and musculoskeletal disorders have entirely distinct pathologies as stated in the prior filed 1.132 declaration of record by Dr. Galer:

3. In contrast to musculoskeletal disorders which are the target pathology in the Petrus reference, Carpal Tunnel Syndrome is not a species of musculoskeletal disorders. Rather, Carpal Tunnel Syndrome is a condition whose symptoms are caused by a disturbance of median nerve function in the wrist as the nerve passes through the carpal tunnel. As such, the pain and symptoms caused by Carpal Tunnel Syndrome do not arise from the musculoskeletal system. Instead, the pain, parasthesia, and dysesthesia arise from direct trauma and dysfunction to the median nerve within the carpal tunnel.

- Because these two conditions arise from entirely distinct pathologies, those of ordinary skill in the art generally treat them differently. See e.g., the following excerpt from the 1.132 declaration of record filed on June 5, 2006:

6. Accordingly, in view of the difference in classification of musculoskeletal disorders and Carpal Tunnel Syndrome, those of skill in the art would approach the treatment of neuropathic pain conditions, of which Carpal Tunnel Syndrome is a member, differently from how they would approach the treatment of musculoskeletal pain disorders. In general, different classes of medications are prescribed for the treatment of neuropathic pain conditions as compared to the treatment of musculoskeletal pain disorders. See for example Exhibits C and D.

a. Exhibit C is an excerpt from an article entitled: Algorithm for Neuropathic Pain Treatment: An Evidence Based Proposal. The article sets forth a comparison of the various treatments used in the amelioration of neuropathic pains. Among the treatments used to remedy neuropathic pains are antidepressants (section 3.2) and anticonvulsants (section 3.3). See Finnerup, N. B. Pain 2005; 118:289-305 at page 290.

b. Exhibit D is an excerpt from the book entitled: Evidenced-Based Management of Acute Musculoskeletal Pain. The excerpt sets forth various treatments recommended for the management of acute musculoskeletal pains. The excerpt specifically points out that there is no evidence that supports the use of anti-depressants or anticonvulsants in the treatment of acute musculoskeletal pain. See page 22.

c. Accordingly, as can be seen with reference to Exhibits C and D, one of skill in the art would approach the treatment of a neuropathic pain differently from how they would approach the treatment of a musculoskeletal pain because in the treatment of a neuropathic pain one of skill in the art may recommend the administration of an anti-depressant or anticonvulsant where as for the treatment of a musculoskeletal pain one would not recommend the administration of an anti-depressant or anticonvulsant.

; and

- There are anatomical reasons why one of ordinary skill in the art would not predict success in the claimed methods without actually performing the method and obtaining positive results. See e.g., the 1.132 declaration filed by Larry Caldwell on April 26, 2005:

In the subject methods, the active agent must cross a barrier to reach the target site to be effective. Barriers are present in the area of the carpal tunnel/median nerve. The carpal tunnel is the interior of the wrist through which the medial nerve, tendons and blood vessels pass. Three sides of the carpal tunnel are bone and the other side is a thickened sheath, the flexor retinaculum, which is made of ligament material. Accordingly, for the subject methods to work, the target agent must cross this bone/ sheath barrier.

Furthermore, the active agent must penetrate deeply in order to reach a target site because carpal tunnel syndrome originates deep within the nerves of the wrist. Prior to my work in reducing the invention to practice, it was not at all certain that a sufficient amount of a given active agent would penetrate deeply enough to reach the target site.

The above facts provide anatomical and physiological reasons why one of skill in the art could not have predicted success in the claimed methods prior to actually performing the methods and obtaining results.

Applicants further establish that there is no predicted success due to the inherent unpredictability present in the chemical art. Courts have viewed the chemical arts as

inherently involving unpredictability.<sup>7</sup> As stated in *Fisher*, chemical reactions and physiological activity involve unpredictable factors.<sup>8</sup>

Edwards teaches treatment of CTS by applying compositions extracted from banana peel. Bockow's methods for treating musculoskeletal diseases employ the inclusion of an omega fatty acid, spirulina, and optionally NSAIDs. Based on these two teachings, the Examiner asserts that treatment of CTS by applying a topical formulation including an NSAID to the palmar dermis is obvious. Like *Fisher*, chemical reactions involving banana peel extracts and a topical formulation including an NSAID, respectively, involve unpredictable factors. Without knowing how an NSAID, when applied to the palmar dermis, would react in the median nerve of the carpal tunnel, treatment of CTS by an NSAID formulation is unpredictable. As such, one of skill in the art could not have predicted success in combining Bockow and Edwards as suggested by the Examiner because Edwards uses banana peel extracts that would involve different chemical reactions than NSAID formulations.

In light of the above analysis, it is respectfully submitted that the Examiner's rejection is flawed because 1) there is no apparent reason to combine teachings of Bockow and Edwards based on the determination of the references at the time of the claimed invention; and 2) one of skill in the art could not have predicted success in practicing the claimed invention in view of the references cited by the Examiner. Consequently, Claims 1-3, 5-8, 10-12, 14-18, 29, 34-36, 38 and 39 are not obvious under 35 U.S.C. §103(a) over Bockow in view of Edwards for many reasons and this rejection may be withdrawn.

#### Rejections of Claims 38 and 39

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<sup>7</sup> *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) ("In cases involving unpredictable factors, such as most chemical reactions and physiological activity, the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved.")

<sup>8</sup> *Id.*

Lastly, Applicants submit that Claims 38 and 39 are not obvious over the cited references because the Examiner did not provide how the claimed elements are necessarily inherent in the prior art.

In rejecting Claims 38 and 39, the Examiner states that the claimed elements (amelioration of symptoms for a period of 1 week or longer for Claim 38 or several weeks or longer for Claim 39) are expected upon successful treatment of CTS and are thus implicitly met by the teachings of the prior art. Office Action, ¶¶ bridging pgs 4 and 5.

Applicants submit that the Examiner did not provide a basis that reasonably supports the determination that, upon the treatment, the symptoms of CTS are necessarily ameliorated for a period of several weeks or longer. The law is clear on this point. "In relying upon the theory of inherency, the examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art."<sup>9</sup> Furthermore, the fact that a certain result or characteristic may occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic.<sup>10</sup>

The Examiner did not provide any reasoning except his conclusion that the claimed elements are inherent upon successful treatment of CTS. Indeed, Bockow indicates that amelioration of the symptoms of a musculoskeletal disorder lasts only up to 24 hours because it teaches application of its formulations 1-4 times daily (col. 7, lines 15-24). As such, Bockow teaches away from the claimed elements that the amelioration lasts for at least 1 week. Consequently, Applicants assert that the rejection of Claims 38 and 39 is further flawed because the Examiner did not provide any basis

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<sup>9</sup> *Ex parte Levy*, 17 USPQ2d 1461, 1464 (Bd. Pat. App. & Inter. 1990) (emphasis in original)

<sup>10</sup> *In re Rijckaert*, 9 F.3d 1531, 1534, 28 USPQ2d 1955, 1957 (Fed. Cir. 1993).



as to its determination that the claimed elements would be necessarily present in the prior art.

***Claim Rejection over Bockow in view of Edwards and Hirano***

Claims 4, 9, and 13 remain rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Bockow (USPN 5,709,855) in view of Edwards (USPN 5,989,559) and Hirano (USPN 5,869,087).

In making this rejection, the Examiner asserts that Bockow in view of Edwards teach all of the elements of the claimed invention but for the topical patch, which element is made up by Hirano. However, as reviewed above, there is no apparent reason to combine teachings of Bockow and Edwards based on the determination of the references at the time of the claimed invention; and Bockow in view of Edwards fails to provide one of skill in the art with the requisite predicted success in the claimed methods. As Hirano was cited solely for the patch element, Hirano fails to make up this deficiency in the primary references and this rejection may be withdrawn.

***Claim Rejection over Bockow in view of Edwards and Shudo***

Claim 19 remains rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Bockow (USPN 5,709,855) in view of Edwards (USPN 5,989,559) and Shudo (US Pub No. 2002/0176886).

As demonstrated above, there is no apparent reason to combine teachings of Bockow and Edwards based on the determination of the references at the time of the claimed invention; and Bockow in view of Edwards do not provide predicted success in the claimed invention. As Shudo was cited for its disclosure of kits containing topical patch formulations and instructions, it fails to remedy the defects of Bockow in view of Edwards. Accordingly, the Applicants respectfully request the Examiner reconsider and withdraw this rejection.

***Claim Rejection over Bockow in view of Edwards, Hirano and a bandage***

Claims 24-28 remain rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Bockow (USPN 5,709,855) in view of Edwards (USPN 5,989,559) and Hirano (U.S. Patent No. 5,869,087) and a bandage.

As demonstrated above, there is no apparent reason to combine teachings of Bockow and Edwards based on the determination of the references at the time of the claimed invention; and Bockow in view of Edwards and Hirano do not provide predicted success in the claimed invention. A bandage does not make up this deficiency. Accordingly, the Applicants respectfully request the Examiner reconsider and withdraw this rejection.

***Claim Rejection over Bockow in view of Edwards and Liebschutz***

Claims 30-33, 37 and 40 are rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Bockow (USPN 5,709,855) in view of Edwards (USPN 5,989,559) and Liebschutz (PCT Pub WO 02/22109).

As demonstrated above, there is no apparent reason to combine teachings of Bockow and Edwards based on the determination of the references at the time of the claimed invention; and Bockow, in view of Edwards, does not provide predicted success in the claimed invention. As Liebschutz was cited for the disclosure of a diclofenac patch, it fails to make up this deficiency. Accordingly, the Applicants respectfully request the Examiner reconsider and withdraw the rejection of Claims 30-33, 37 and 40.

Furthermore, Applicants submit that Claim 37 is not obvious over the cited references because there is no predicted success in the claimed topical NSAID formulation comprising from about 0.5 to 2% w/w of an active NSAID agent.

In rejecting this claim, the Examiner asserts Liebschutz discloses a patch containing diclofenac in an amount from 1% to 5%.

However, Liebschutz provides three examples in which the patches contain 2.5-3% of diclofenac. Furthermore, Bockow teaches away from a topical formulation containing 0.5 to 2% of NSAID because it discloses examples in which the topical formulations all contain 3-25% of NSAID. As such, upon reading Liebschutz and Bockow, one of skill in the art would be motivated to include at least 3% of NSAID in producing a topical NSAID formulation.

Consequently, Bockow in view of Liebschutz additionally fails to provide predicted success in Claim 37. Accordingly, the Applicants further request that the Examiner reconsider and withdraw the rejection of Claim 37.

Applicants submit that Claim 40 is not obvious over the cited references because Bockow teaches away from topical NSAID formulations comprising an NSAID as the only active agent and would be rendered unsatisfactory for its intended purpose if modified as proposed by the Examiner.

It appears that the Examiner attempts to eliminate the omega fatty acid and spirulina from Bockow's formulation, alleging that Liebschutz teaches a patch containing diclofenac as the only active agent. By combining the teachings of Bockow and Liebschutz, the Examiner modifies Bockow's formulation so that an NSAID becomes the only active agent as recited in Claim 40.

However, Bockow teaches away from a topical formulation comprising an NSAID as the only active agent because Bockow's formulation requires the presence of an omega fatty acid and spirulina, both as active agents. Bockow teaches that the inclusion of NSAIDs is optional. References cannot be combined if the references teach away from their combination. *In re Grasselli*, 713 F.2d 731, 743, 218 USPQ 769, 779 (Fed. Cir. 1983). As such, contrary to the Examiner's assertion, Bockow and Liebschutz cannot be combined.

Furthermore, the inclusion of an omega fatty acid and spirulina in its formulation is central to Bockow. Per Bockow, an omega fatty acid is a known inhibitor of inflammation (col. 1, lines 65-67) and spirulina is known for providing numerous health benefits (col. 4, line 61 to col. 5, line 14). Since the inclusion of an omega fatty acid and spirulina is key to the success of Bockow's formulation, the omega fatty acid and spirulina cannot be eliminated from its formulation without rendering Bockow inoperable and unsuitable for its intended purpose. As such, the proposed modification would render Bockow unsatisfactory for its intended purpose. If a proposed modification would render the prior art invention being modified unsatisfactory for its intended purpose, then there is no suggestion or motivation to make the proposed modification. *In re Gordon*, 733 F.2d 900, 221 USPQ 1125 (Fed. Cir. 1984). Thus, Bockow provides no suggestion or motivation to make the modification proposed by the Examiner.

Consequently, Claim 40 is additionally distinguished over Bockow in view of Liebschutz. Accordingly, the Applicants further request that the Examiner reconsider and withdraw the rejection of Claim 40.

**CONCLUSION**

The Applicants submit that all of the claims are in condition for allowance, which action is requested. If the Examiner finds that a telephone conference would expedite the prosecution of this application, please telephone the undersigned at the number provided.

The Commissioner is hereby authorized to charge any underpayment of fees associated with this communication, including any necessary fees for extensions of time, or credit any overpayment to Deposit Account No. 50-0815, order number CALD-005.

Respectfully submitted,  
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Date: May 27, 2008

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